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=> d his

     (FILE 'HOME' ENTERED AT 08:44:52 ON 10 JUN 2003)

     FILE 'CA' ENTERED AT 08:45:02 ON 10 JUN 2003
L1       148813 S THROMBIN OR EDTA OR HEPARIN OR HIRUDIN OR ATIII OR (PROTEIN C
L2        20340 S VENOM OR ECARIN
L3         1966 S L1 AND L2
L4       918280 S ANST/RL
L5          184 S L3 AND L4
L6            2 S ?NITOANILIDE
L7         4188 S ?NITROANILIDE
L8            9 S ?NITROANILIN
L9         4197 S L7 OR L8
L10           9 S L9 AND L5
L11        2716 S THROMBIN INHIBITOR
L12     2331760 S TEST OR DETERMINATION
L13          54 S L12 (3A) L11
L14          91 S L2 AND L9
L15      140369 S ANTITHROMBIN OR CHELATOR OR EDTA OR HEPARIN OR HIRUDIN OR (PR
L16          36 S L14 AND L15
L17           0 S L13 AND L16
L18        1005 S ((THROMBIN INHIBITOR) OR (INHIBITION OF THROMBIN))/TI
L19     2634722 S L12 OR L4
L20          93 S L19 AND L18

     FILE 'WPIDS' ENTERED AT 10:20:42 ON 10 JUN 2003
L21         274 S L18
L22          39 S L12 AND L21

     FILE 'USPATFULL' ENTERED AT 10:27:04 ON 10 JUN 2003
L23       80529 S ANTITHROMBIN OR EDTA OR HEPARIN OR PROTEIN C OR HIRUDIN
L24       19994 S CHROMOGENIC OR ?NITROANILINE OR ?NITROANILIDE
L25        4484 S ECARIN OR VENOM
L26         598 S L23 AND L24 AND L25
L27          20 S L23 (P) L24 (P) L25

=> log hold
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    14.66     310.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -25.42

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:30:57 ON 10 JUN 2003
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=> d bib ab ind 1-9

L10 ANSWER 1 OF 9 CA COPYRIGHT 2003 ACS
AN 131:112958 CA
TI CA-1 method, a novel assay for quantification of normal prothrombin using a Ca2+-dependent prothrombin activator, carinactivase-1
AU Yamada, Daisuke; Morita, Takashi
CS Department of Biochemistry, Meiji Pharmaceutical University, Tokyo, 204-8588, Japan
SO Thrombosis Research (1999), 94(4), 221-226
CODEN: THBRAA; ISSN: 0049-3848
PB Elsevier Science Inc.
DT Journal
LA English
AB We established a novel prothrombin assay, designated CA-1 method, for quantification of normal prothrombin in application of a Ca2+-dependent prothrombin activator, carinactivase-1 (CA-1), found in the **venom** of Echis carinatus leucogaster. On microplate, **thrombin** converted from normal prothrombin in plasma sample by CA-1 cleaves a **thrombin** specific chromogenic substrate, t-butoxy-Val-Pro-Arg-p-**nitroanilide** and liberates p-nitro-aniline. Then, the normal prothrombin level is decided by measuring the velocity of p-nitroaniline liberation. Normal prothrombin levels in plasma from warfarin-treated individuals were highly correlated with coagulant activities assayed by both prothrombin time and thrombotest. CA-1 method is not only a rapid and highly sensitive chromogenic microplate assay for quantification of normal prothrombin in the range of 10-200 ng/100 .mu.l in plasma samples but also suitable for analyses of many samples in a short time. In addn., normal prothrombin levels obtained by CA-1 method are not inhibited by **EDTA** and **heparin**, which reduce prothrombin time and thrombotest activities. CA-1 method is a novel assay for monitoring coagulant activity in warfarin-treated individuals.
CC 7-1 (Enzymes)
Section cross-reference(s): 13
ST prothrombin detn blood warfarin therapy
IT Blood analysis
Blood coagulation
(the CA-1 method is a novel assay for quantification of normal prothrombin using the Ca2+-dependent prothrombin activator carinactivase-1)
IT 9001-26-7, Prothrombin
RL: ANT (Analyte); **ANST (Analytical study)**
(the CA-1 method is a novel assay for quantification of normal prothrombin using the Ca2+-dependent prothrombin activator carinactivase-1)
IT 174632-07-6, Carinactivase-1
RL: ARG (Analytical reagent use); **ANST (Analytical study)**; USES (Uses)
(the CA-1 method is a novel assay for quantification of normal prothrombin using the Ca2+-dependent prothrombin activator carinactivase-1)
IT 81-81-2, Warfarin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(the CA-1 method is a novel assay for quantification of normal prothrombin using the Ca2+-dependent prothrombin activator carinactivase-1)
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 9 CA COPYRIGHT 2003 ACS
AN 126:222061 CA
TI A rapid and highly sensitive chromogenic microplate assay for quantification of rat and human prothrombin

AU Rob, Jan A.; Tollefsen, Stig; Helgeland, Liv
CS Dep. Biochemistry, Univ. Oslo, Oslo, 0316, Norway
SO Analytical Biochemistry (1997), 245(2), 222-225
CODEN: ANBCA2; ISSN: 0003-2697
PB Academic
DT Journal
LA English
AB A rapid and highly sensitive chromogenic microplate assay for quantification of rat and human prothrombin in subcellular fractions and large series of plasma samples has been developed. The assay is based on the conversion of prothrombin to **thrombin**, using Echis carinatus **venom** as an activator, and the subsequent cleavage of a chromogenic **thrombin** specific substrate, D-cyclohexylglycyl-L-alanyl-L-arginine-p-**nitroanilide** dihydroacetate. Para-Nitroaniline being released by the cleavage is then measured at 410 nm with a microplate reader. The method is suitable for analyses of a large no. of samples in a short time, measuring prothrombin in the nanogram range (0.3-2.4 ng/40 .mu.l of sample).
CC 7-1 (Enzymes)
ST prothrombin detn
IT 9001-26-7, Prothrombin
RL: ANT (Analyte); **ANST (Analytical study)**
(highly sensitive chromogenic microplate assay for quantification of rat and human prothrombin)

L10 ANSWER 3 OF 9 CA COPYRIGHT 2003 ACS
AN 119:199151 CA
TI Protein S chromogenic assay
IN Van De Waart, Piet; Woodhams, Barry J.
PA Baxter Diagnostics Inc., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9310262	A1	19930527	WO 1992-US9971	19921120
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	US 5308756	A	19940503	US 1991-796032	19911120
	CA 2100567	AA	19930521	CA 1992-2100567	19921120
	CA 2100567	C	19970930		
	AU 9331423	A1	19930615	AU 1993-31423	19921120
	AU 651024	B2	19940707		
	EP 567636	A1	19931103	EP 1992-925327	19921120
	EP 567636	B1	19970108		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, SE				
	JP 06504682	T2	19940602	JP 1992-509514	19921120
	AT 147439	E	19970115	AT 1992-925327	19921120
	ES 2097373	T3	19970401	ES 1992-925327	19921120
PRAI	US 1991-796032		19911120		
	WO 1992-US9971		19921120		

AB Free (functional) protein S, which inactivates coagulation factor VIII, is detd. in the blood by (1) eliminating the protection of factor VIII by von Willebrand's factor (vWF) in the sample; (2) adding a predetd. amt. of factor VIII, activated **protein C** (in an amt. sufficient to inactivate a portion of the factor VIII), phospholipids, and Ca2+ and incubating; (3) adding factor II, factor IXa, factor X, and Ca2+ (and **thrombin** inhibitor) in amts. sufficient to activate the factor X in the presence of activated factor VIII; (4) adding a chromogenic substrate which is cleaved by factor Xa; (5) measuring the color produced as an indirect measure of free protein S, whose concn. in the reaction mixt. is directly correlated to the amt. of factor VIII that

is inactivated. The vWF effect on factor VIII may be eliminated with an anti-vWF antibody, inactivated factor VIII or factor VIII fragments that bind to vWF, synthetic peptides that prevent vWF interaction with factor VIII, or vWF-degrading enzymes. Thus, 25 .mu.L sample and 25 .mu.L Tris buffer (pH 8.0) in a microtiter plate well was incubated sequentially with (1) activated **protein C**, phospholipid, CaCl2, anti-vWF, PEG 6000, albumin, and NaCl, (2) a support reagent contg. lyophilized bovine factor VIII, (3) factors IXa, X, and IIa in MES buffer, and (4) MeO2C-D-cyclohexylarginine-Gly-Arg p-**nitroanilide** in the presence of N.alpha.-(2-naphthylsulfonylglycyl)-DL-amidinophenylalanine piperidide (**thrombin** inhibitor), and the absorbance was measured at 405 nm.

IC ICM C12Q001-56
ICS G01N033-86

CC 9-5 (Biochemical Methods)

ST protein S detn blood coagulation

IT Phosphatidylcholines, uses
Phosphatidylserines
Phospholipids, uses
RL: USES (Uses)
(in protein S detn., in body fluid, spectrophotometric)

IT Snake
(**protein C** activator of **venom** of, in protein S spectrophotometric detn. in body fluid)

IT **Venoms**
(**protein C** activator of, of snake, in protein S spectrophotometric detn. in body fluid)

IT Antibodies
RL: **ANST (Analytical study)**
(to von Willebrand's factor, in protein S spectrophotometric detn. in body fluid)

IT Peptides, uses
RL: USES (Uses)
(von Willebrand's factor interaction with blood-coagulation factor VIII prevention by, in protein S spectrophotometric detn. in body fluid)

IT Blood-coagulation factors
RL: ANT (Analyte); **ANST (Analytical study)**
(protein S, detn. of, in body fluid, spectrophotometric)

IT 9002-04-4, Blood-coagulation factor IIa
RL: **ANST (Analytical study)**
(and inhibitor of, in protein S detn., in body fluid, spectrophotometric)

IT 117091-16-4 7440-70-2, Calcium, uses 9001-27-8, Blood-coagulation factor VIII 9001-29-0, Blood-coagulation factor X 10043-52-4, Calcium chloride, uses 37316-87-3, Blood-coagulation factor IXa 60202-16-6, Blood-coagulation factor XIV 80895-09-6
RL: **ANST (Analytical study)**
(in protein S detn., in body fluid, spectrophotometric)

IT 109319-16-6, Von Willebrand's factor
RL: **ANST (Analytical study)**
(removal of interference from, in protein S spectrophotometric detn. in body fluid)

IT 9001-92-7, Proteinase
RL: RCT (Reactant); RACT (Reactant or reagent)
(von Willebrand's factor hydrolysis by, in protein S spectrophotometric detn. in body fluid)

L10 ANSWER 4 OF 9 CA COPYRIGHT 2003 ACS

AN 114:2469 CA

TI Comparison of amidolytic, ELISA (enzyme-linked immunosorbent assay) and coagulation assays for the determination of **protein C** in the normal and abnormal plasma

AU Tanaka, Yumiko; Kawada, Tsutomu; Ono, Hitoshi; Ohtagawa, Kazumi; Seki, Tsugumi; Shiba, Takako; Ikeda, Masakatsu; Ichikawa, Yukinobu; Fusegawa,

Hisae; Andoh, Yasuhiko
CS Sch. Med., Tokai Univ. Hosp., Isehara, Japan
SO Rinsho Kensa (1990), 34(2), 231-6
CODEN: RNKNAT; ISSN: 0485-1420
DT Journal
LA Japanese
AB The plasma **protein C** (PC) activity was detd. by an amidalytic assay kit in which the plasma PC was activated by a snake **venom** PC activator, the activated PC was incubated with substrate p-Glu-Pro-Arginyl **methoxynitroanilide**, and the released **methoxynitroanilide** was measured at 405 nm to obtain the PC activity. The amidolytic assay for the plasma PC showed good reproducibility (intrassay relative std. derivation 1.5-6.4%) and was not affected by the bilirubin, Hb, and lipids present in plasma samples. The plasma PC level detd. by the amidolytic assay was comparable to that detd. by ELISA and and coagulation assay, indicating that the amidolytic assay is suitable for use in plasma PC monitoring for diagnosis of diseases such as hepatic diseases (cirrhosis) and disseminated intravascular coagulation.
CC 7-1 (Enzymes)
Section cross-reference(s): 14
ST **protein C** detn blood plasma; amidolytic assay
protein C plasma
IT 60202-16-6, **Protein C**
RL: ANT (Analyte); **ANST (Analytical study)**
(detn. of, of blood plasma by amidolytic and ELISA and coagulation assays)
IT 130835-45-9
RL: BIOL (Biological study)
(in **protein C** detn. in blood plasma)

L10 ANSWER 5 OF 9 CA COPYRIGHT 2003 ACS
AN 112:72942 CA
TI Snake **protein C** activator, methods of preparation and use thereof
IN Stocker, Kurt F.; Svendsen, Lars G.
PA Pentapharm A.-G., Switz.
SO U.S., 11 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4849403	A	19890718	US 1986-861786	19860509
	AU 8657369	A1	19861204	AU 1986-57369	19860513
	AU 605462	B2	19910117		
	DK 8602248	A	19861130	DK 1986-2248	19860514
	DK 165199	B	19921019		
	DK 165199	C	19930301		
	IL 78829	A1	19900831	IL 1986-78829	19860519
	NO 8602118	A	19861201	NO 1986-2118	19860528
	NO 166303	B	19910318		
	NO 166303	C	19910626		
	ES 555428	A1	19871201	ES 1986-555428	19860528
	CA 1286223	A1	19910716	CA 1986-510137	19860528
	JP 61280298	A2	19861210	JP 1986-122398	19860529
	JP 07036760	B4	19950426		
	ES 557670	A1	19880716	ES 1987-557670	19870814
	ES 557670	A5	19880809		
PRAI	CH 1985-2267		19850529		
	CH 1985-4135		19850925		
	CH 1985-5087		19851128		

OS MARPAT 112:72942

AB A **protein C** activator is purified from the **venom** of Agkistrodon contortrix or from other snake **venoms** contg. immunol. cross reacting-material by chromatog. The activator is used to assay for **protein C**, to prevent or treat thrombotic disorders, and to obtain activated **protein C** from **protein C**-contg. aq. media. The activator may also be obtained by culturing a recombinant microorganism contg. .gtoreq.1 gene for the activator. Chromogenic peptide substrates for measuring activated **protein C** are also described. A. contortrix **venom** was pretreated by dissolving it in H2O, adjusting the pH to 3.0, incubating the soln. at 70.degree. for 10 min, cooling to 20.degree., adjusting the pH to 7.2, and centrifuging the resultant turbid soln. The residue was dissolved in H2O and chromatographed on DEAE-Sephadex A-50, CM-Sephadex C-50, and Sephadex G-100 to give pure **protein C** activator. In a photometric assay of **protein C**, human citrated plasma was incubated with the activator and activated **protein-C** was detd. using 2AcOH.H-D-CHG-L-Pro-L-Arg-pNA (CHG = cyclohexylglycine, pNA = p-**nitroanilide**) as chromogenic substrate and measuring absorbance at 405 nm.

IC ICM A61K037-00

NCL 514002000

CC 7-3 (Enzymes)
Section cross-reference(s): 1, 9, 12, 16

ST **protein C** activator Agkistrodon **venom**; antithrombotic **protein C** activator Agkistrodon; blood analysis **protein C** Agkistrodon activator; peptide substrate activated **protein C**

IT Microorganism
(cloning in, of gene for **protein C** activator of Agkistrodon contortrix)

IT Organ
(exts., **protein C** detn. in, activator from Agkistrodon contortrix **venom** for)

IT Gene and Genetic element, animal
RL: PROC (Process)
(for **protein C** activator of Agkistrodon contortrix, cloning of)

IT Molecular cloning
(of gene for **protein C** activator of Agkistrodon contortrix)

IT Agkistrodon contortrix
Snake
(**protein C** activator of **venom** of)

IT Anticoagulants and Antithrombotics
(**protein C** activator of Agkistrodon contortrix)

IT Animal tissue culture
(**protein C** detn. in, activator from Agkistrodon contortrix **venom** for)

IT **Venoms**
(snake, **protein C** activator of, purifn. of)

IT Peptides, compounds
RL: BIOL (Biological study)
(conjugates, with chromogen, in **protein C** photometric detn. with activator from Agkistrodon contortrix **venom**)

IT Peptides, compounds
RL: BIOL (Biological study)
(synthetic, conjugates, with chromogen, in **protein C** photometric detn. with activator from Agkistrodon contortrix **venom**)

IT 68987-32-6DP, **protein C** activator reaction products
RL: PREP (Preparation)
(activated **protein C** manuf. from **protein**

C with)
IT 98530-77-9
RL: ANT (Analyte); **ANST (Analytical study)**
(detn. of, activator from Agkistrodon contortrix **venom** for)
IT 74-79-3, L-Arginine, biological studies
RL: BIOL (Biological study)
(di- or tripeptides contg. carboxy-terminal, in **protein C** detn. by activator from Agkistrodon contortrix **venom**)
IT 72194-57-1 77672-32-3 88927-41-7 102565-94-6 108963-65-1 108963-69-5
RL: BIOL (Biological study)
(in **protein C** photometric detn. with activator from Agkistrodon contortrix **venom**)
IT 42617-41-4P, Activated **protein C**
RL: PREP (Preparation)
(prepn. of, from **protein C** zymogen, with activator from Agkistrodon contortrix **venom**)
IT 9001-24-5, Blood-coagulation factor V 9001-27-8, Blood-coagulation factor VIII
RL: BIOL (Biological study)
(**protein C** detn. by activator from Agkistrodon contortrix **venom** in relation to)

L10 ANSWER 6 OF 9 CA COPYRIGHT 2003 ACS
AN 111:92852 CA
TI New **protein C** activator and its use in **protein C** determination in body fluids
IN Orthner, Carolyn
PA American National Red Cross, USA
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 8900205	A1	19890112	WO 1988-US2278	19880705
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4908314	A	19900313	US 1987-69496	19870702
PRAI US 1987-69496		19870702		

AB A **protein C** activator from the **venom** of the southern copperhead snake, its use in detg. **protein C** in a body sample, and a test kit contg. the **protein C** activator are described. The **venom** was dialyzed and chromatographed on SP-Sephadex C-50, S-200 Sephacryl, and then G-100 Sephadex to give an active fraction with 64-fold purifn. For detn. of functional **protein C** in blood plasma, a sample was incubated in a pH 7.5 buffer contg. 5.5 mM **EDTA** and polyethylene glycol (1 mg/mL) at 30.degree. and to this was added **protein C** activator (final concn. 92 nM). After 10 min incubation, soybean trypsin inhibitor was added, followed by adding NaCl (to 0.13 M) and L-pyroglutamyl-L-prolyl-L-arginine-p-**nitroanilide** and spectrophotometric anal. at 410 nm.
IC ICM C12Q001-56
ICS C12N009-50; A61K037-547
CC 7-2 (Enzymes)
Section cross-reference(s): 9
ST **protein C** activator isolation characterization; snake **venom protein C** activator isolation; plasma **protein C** detn activator
IT Agkistrodon contortrix
(**protein C** activator of **venom** of, purifn.

and properties of)
IT **Venoms**
(**protein C** activator of, of Southern copperhead snake, purifn. and properties of)
IT Proteins, specific or class
RL: ANT (Analyte); **ANST (Analytical study)**
(C, detn. and activation of, with **protein C** activator from snake **venom**)
IT 111174-52-8
RL: BIOL (Biological study)
(isolation and characterization and anal. and therapeutic use of)
IT 42617-41-4P, Activated **protein C**
RL: PREP (Preparation)
(prepn. of, from **protein C** activator with **protein C** activator)
IT 9035-81-8, Trypsin inhibitor 72194-57-1
RL: BIOL (Biological study)
(**protein C** detn. with reagents contg. **protein C** activator and)

L10 ANSWER 7 OF 9 CA COPYRIGHT 2003 ACS
AN 107:35685 CA
TI Quantitative determination of **protein C** and activator preparation for its implementation
IN Stocker, Kurt F.; Svendsen, Lars G.
PA Pentapharm A.-G., Switz.
SO Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 203509	A2	19861203	EP 1986-106881	19860521
	EP 203509	A3	19881005		
	EP 203509	B1	19910403		
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
	AU 8657369	A1	19861204	AU 1986-57369	19860513
	AU 605462	B2	19910117		
	DK 8602248	A	19861130	DK 1986-2248	19860514
	DK 165199	B	19921019		
	DK 165199	C	19930301		
	IL 78829	A1	19900831	IL 1986-78829	19860519
	AT 62274	E	19910415	AT 1986-106881	19860521
	NO 8602118	A	19861201	NO 1986-2118	19860528
	NO 166303	B	19910318		
	NO 166303	C	19910626		
	ES 555428	A1	19871201	ES 1986-555428	19860528
	CA 1286223	A1	19910716	CA 1986-510137	19860528
	JP 61280298	A2	19861210	JP 1986-122398	19860529
	JP 07036760	B4	19950426		
	ES 557670	A1	19880716	ES 1987-557670	19870814
	ES 557670	A5	19880809		
PRAI	CH 1985-2267		19850529		
	CH 1985-4135		19850925		
	CH 1985-5087		19851128		
	EP 1986-106881		19860521		

AB **Protein C** is detd. in plasma or other samples by activation with snake **venom**, followed by incubation of the activated **protein C** (i.e. proteolytically active protein Ca) with a chromogenic oligopeptide substrate R2-D-NHCH[(CH2)NHR3]CO-L-Pro-L-Arg-R1 [R1 = NHC6H3NO2-4, NHC10H7; R2 = H, C2-6 alkanoyl, alkoxycarbonyl, C1-2 alkylsulfonyl, (substituted) benzoyl, (substituted) benzyloxycarbonyl, etc.; R3 = R2, amidino, tosylamidino; n =

3,4] and photometric detn. of the cleavage products. The **venom**, from Agkistrodon contortix, contains a **protein C** activator which is useful as an antithrombotic. This activator was purified from **venom** by chromatog. on DEAE-Sephadex A-50 and used for detn. for **protein C** in citrated human plasma with D-cyclohexylglycyl-L-prolyl-L-arginine p-**nitroanilide**-2AcOH as substrate for the protein C2 formed. The **protein C** activated from **venom** did not coagulate fibrinogen, did not lyse fibrin, and was not inhibited by antithrombin III, **heparin**, **hirudin**, or aprotinin. It had a mol. wt. of about 39,000, and isoelec. point of 3.0, and a carbohydrate content of 20%.

IC ICM C12Q001-38
ICA C12Q001-56; G01N033-86; A61K035-38; G01N033-68
CC 7-1 (Enzymes)
Section cross-reference(s): 1
ST **protein C** detn plasma; Agkistradon **venom**
protein C activator; snake **venom**
protein C activator
IT Peptides, uses and miscellaneous
RL: USES (Uses)
(chromogenic, for **protein C** detn., activator from snake **venom** in relation to)
IT Agkistrodon contortrix
Snake
(**protein C** activator of **venom** of)
IT **Venoms**
(**protein C** activator of, of snake)
IT Escherichia coli
Microorganism
Saccharomyces cerevisiae
(**protein C** detn. in genetically engineered, activator from snake **venom** in)
IT Animal tissue culture
Organ
(**protein C** detn. in, activator from snake **venom** in)
IT Blood analysis
(**protein C** detn. in, of human and other mammals, activator from snake **venom** in)
IT 86890-95-1 88927-41-7 102565-94-6 108963-64-0 108963-66-2
108963-67-3 108963-68-4 108963-70-8 108963-71-9 108963-72-0
108963-74-2 108998-14-7
RL: BIOL (Biological study)
(as chromogenic substrate, in **protein C** detn., activator from snake **venom** in relation to)
IT 60202-16-6, Blood-coagulation factor XIV
RL: ANT (Analyte); **ANST (Analytical study)**
(detn. of, activator from snake **venom** in)
IT 42617-41-4, Blood-coagulation factor XIVa
RL: FORM (Formation, nonpreparative)
(formation of, **protein C** activator from snake **venom** in)

L10 ANSWER 8 OF 9 CA COPYRIGHT 2003 ACS
AN 105:2520 CA
TI Comparison of two methods for proteolytic enzyme detection in snake **venom**
AU Markland, Francis S., Jr.; Perdon, Alicia
CS Sch. Med., Univ. South. California, Los Angeles, CA, 90033, USA
SO Toxicon (1986), 24(4), 385-93
CODEN: TOXIA6; ISSN: 0041-0101
DT Journal
LA English
AB An acrylamide gel system contg. fibrinogen was used to detect proteolytic

enzymes in snake **venom**. Proteolytic activity was obsd. as a clear area on a blue background after electrophoresis and overnight incubation in Tris buffer, prior to staining with Coomassie Blue. **Venoms** from eastern and western diamondback and west coast Mexican rattlesnakes, Crotalus adamanteus, C. atrox, and C. basiliscus basiliscus, resp., and southern copperhead, Agkistrodon contortrix contortrix, were analyzed at the level of 1 mg of **venom**. The effects of the serine proteinase inhibitor, diisopropyl fluorophosphate (DFP), and the metalloproteinase inhibitors, tetraethylenepentamine (TEP) or **EDTA**, on fibrinogen and normal gel profiles were evaluated. Normal gels (without fibrinogen) were stained with Coomassie Blue to visualize the migration of 250 .mu.g of **venom** proteins on the gels. Several proteolytic enzymes detected in C. atrox and C. basiliscus **venoms** were inhibited by TEP, whereas DFP had no effect on activity. The fibrinogen gels detected no proteinase activity in C. adamanteus **venom**, although it is known from other studies that there are several proteolytic enzymes in this **venom**. Several proteinases were detected in A. contortrix contortrix **venom**, one of which was inhibited by TEP. By comparison, proteolytic activity in 5-10 .mu.g of all **venoms** was readily detected using the mammalian kallikrein specific chromogenic substrate, S 2302 (H-D-Pro-Phe-Arg-p-**nitroanilide**). Thus, the fibrinogen gel method does not appear to have the specificity nor the sensitivity of the recently developed chromogenic substrates for the detection of proteolytic enzymes in snake **venom**.

CC 7-1 (Enzymes)

ST proteinase detection snake **venom**

IT Fibrinogens
RL: BIOL (Biological study)
(polyacrylamide gels contg., snake **venom** proteinase detection on)

IT Agkistrodon contortrix contortrix
(proteinase of **venom** of, detection of)

IT Crotalus
Snake
(proteinases of **venoms** of, detection of)

IT **Venoms**
(proteinases of, of snakes, detection of)

IT 9001-01-8 9002-04-4
RL: BIOL (Biological study)
(detection of serine proteinases of snake **venom** related to, comparison of methods for)

IT 56467-79-9
RL: ANT (Analyte); **ANST (Analytical study)**
(detection of, comparison of methods for)

IT 9001-92-7 81669-70-7
RL: ANT (Analyte); **ANST (Analytical study)**
(detection of, in snake **venom**, comparison of methods for)

IT 64816-19-9
RL: BIOL (Biological study)
(in detection of proteinases of snake **venom**)

L10 ANSWER 9 OF 9 CA COPYRIGHT 2003 ACS

AN 90:164243 CA

TI A highly sensitive assay of platelet factor 3 using a chromogenic substrate

AU Sandberg, Helena; Andersson, Lars Olov

CS Res. Dep., AB Kabi, Stockholm, Swed.

SO Thrombosis Research (1979), 14(1), 113-24
CODEN: THBRAA; ISSN: 0049-3848

DT Journal

LA English

AB A sensitive method for detn. of platelet factor 3 (PF 3) is described in which **thrombin** generation is measured in a mixt. of prothrombin

complex conc., Russell's viper **venom**, Ca2+, and the sample contg. PF 3 activity. **Thrombin** generation is detd. spectrometrically by using a chromogenic synthetic peptide H-D-Phe-Pip-Arg-p-**nitroanilide** (S-2238), as a substrate for **thrombin**. The assay is .apprx.10-fold as sensitive as the Stypven clotting time, commonly used to det. PF 3. Detns. in normal blood donors showed varying levels of PF 3 activity that seemed to be individually related. For most individuals, the values obtained were essentially the same from 1 occasion to another.

CC 9-4 (Biochemical Methods)
Section cross-reference(s): 13

ST blood platelet factor 3 detn; spectrometry platelet factor 3; plasma platelet factor 3 detn

IT Blood analysis
(blood platelet factor 3 detn. in, spectrometric, chromogenic substrate for)

IT 62354-65-8
RL: **ANST (Analytical study)**
(chromogenic substrate, for blood platelet factor 3 spectrometric detn.)

IT 37270-93-2
RL: ANT (Analyte); **ANST (Analytical study)**
(detn. of, in blood plasma, spectrometric, chromogenic substrate for)

L20 ANSWER 22 OF 93 CA COPYRIGHT 2003 ACS
AN 133:132122 CA
TI Method for determining the concentration of **thrombin inhibitors** using spectrophotometry
IN Nowak, Gotz; Bucha, Elke
PA Haemosys G.m.b.H., Germany
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000046602	A2	20000810	WO 2000-DE330	20000128
	WO 2000046602	A3	20001116		
	W: AE, AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19904674	A1	20000831	DE 1999-19904674	19990204
	EP 1149173	A2	20011031	EP 2000-912349	20000128
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002536642	T2	20021029	JP 2000-597633	20000128
PRAI	DE 1999-19904674	A	19990204		
	WO 2000-DE330	W	20000128		

AB The invention relates to a method for detg. the concn. of thrombin inhibitors in a non-turbid body fluid or a non-turbid ext. from a body fluid. The body fluid is taken from a living organism and is sepd., if required, from the turbidities. An anticoagulative agent that does not affect the prothrombin/active meizothrombin or Mtdesfg1 conversion process, a chromogenic or fluorogenic substrate that can be cleaved by active meizothrombin or Mtdesfg1 and a substance that cleaves prothrombin into meizothrombin or Mtdesfg1, in addn. to prothrombin (optionally) are added to the non-turbid body fluid thus obtained. The mixt. thus obtained undergoes time-based wavelength-selective light absorption or light emission measurement. The amt. of thrombin inhibitor contained in the body fluid is detd. by means of comparison with detd. std. curves on the basis of a decrease in the absorption or emission of light.

IC ICM G01N033-86
CC 9-5 (Biochemical Methods)
Section cross-reference(s): 1, 14
ST thrombin inhibitor **detn** spectrophotometry ecarin prothrombin meizothrombin hirudin nitroaniline
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PIVKA, protein induced by Vitamin K antagonist; method for detg. concn. of thrombin inhibitors using spectrophotometry)
IT Anticoagulants
Blood analysis
Blood coagulation
Body fluid
Cerebrospinal fluid
Color formers
Saliva
Test kits
Transparency

UV and visible spectroscopy
Urine analysis
(method for detg. concn. of thrombin inhibitors using spectrophotometry)

IT Venoms
(snake; method for detg. concn. of thrombin inhibitors using spectrophotometry)

IT 100-01-6, p-Nitroaniline, uses 55466-26-7, Ecarin 133876-35-4, Pefachrome TH
RL: ARG (Analytical reagent use); **ANST (Analytical study)**; USES (Uses)
(method for detg. concn. of thrombin inhibitors using spectrophotometry)

IT 7440-70-2D, Calcium, complexes, analysis 9000-94-6, Antithrombin 9005-49-6, Heparin, analysis 60202-16-6, Blood-coagulation factor XIV
RL: ARU (Analytical role, unclassified); **ANST (Analytical study)**
(method for detg. concn. of thrombin inhibitors using spectrophotometry)

IT 8001-27-2, Hirudin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(method for detg. concn. of thrombin inhibitors using spectrophotometry)

IT 9002-04-4, Thrombin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(method for detg. concn. of thrombin inhibitors using spectrophotometry)

IT 9001-26-7, Prothrombin 69346-19-6, Meizothrombin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(method for detg. concn. of thrombin inhibitors using spectrophotometry)

=>

L13 ANSWER 1 OF 54 CA COPYRIGHT 2003 ACS
AN 138:283166 CA
TI **Determination** of trypsin and **thrombin inhibitors** in water bloom from Taihu Lake
AU Ao, Zonghua; Tao, Wenyi; Tang, Xiaozhi; Sun, Wei; Xu, Zhenghong
CS School of Biotechnology, Southern Yangtze University, Wuxi, 214036, Peop. Rep. China
SO Wuxi Qinggong Daxue Xuebao (2002), 21(3), 305-306, 309
CODEN: WQDXF3; ISSN: 1009-038X
PB Wuxi Qinggong Daxue Xuebao Bianjibu
DT Journal
LA Chinese
AB The trypsin and thrombin inhibitors in water bloom from Taihu Lake were studied by chromatog. and the detection of inhibition enzyme activity. The results showed that a few kinds of trypsin inhibitors and thrombin inhibitors were found in the water bloom from Taihu Lake.
CC 7-3 (Enzymes)
Section cross-reference(s): 10
ST trypsin **thrombin inhibitor detn** water bloom
IT Microcystis
(**detn**. of trypsin and **thrombin inhibitors** in water bloom)
IT 9000-94-6, **Thrombin inhibitor** 9035-81-8, Trypsin inhibitor
RL: ANT (Analyte); ANST (Analytical study)
(**detn**. of trypsin and **thrombin inhibitors** in water bloom)

L13 ANSWER 11 OF 54 CA COPYRIGHT 2003 ACS
AN 123:107245 CA
TI Method for determination of thrombocyte aggregation
IN Reers, Martin
PA Behringwerke A.-G., Germany
SO Eur. Pat. Appl., 5 pp
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 661383	A2	19950705	EP 1994-119803	19941215
	EP 661383	A3	19971217		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	DE 4344919	A1	19950706	DE 1993-4344919	19931230
	AT 199939	E	20010415	AT 1994-119803	19941215
	ES 2155842	T3	20010601	ES 1994-119803	19941215
	CA 2138931	AA	19950701	CA 1994-2138931	19941222
	JP 07203994	A2	19950808	JP 1994-326514	19941228
	AU 9481788	A1	19950706	AU 1994-81788	19941229
	AU 702099	B2	19990211		
	US 5563041	A	19961008	US 1994-365759	19941229
PRAI	DE 1993-4344919	A	19931230		

AB A diagnostic test for thrombin-induced platelet aggregation in the presence of fibrin uses a fibrin aggregation inhibitor to prevent interference from formation of a fibrin clot. This method can be used for qual. or quant. detn. of the platelet aggregation-inhibiting activity of thrombin inhibitors present simultaneously with the inhibitor of fibrin aggregation. Thus, a mixt. of 300 .mu.L citrate-anticoagulated plasma, 100 .mu.L tri-Na citrate dihydrate soln. (380 mg/100 mL), 25 .mu.L fibrin aggregation inhibitor soln. (1 g albumin and 10 g Gly-Pro-Arg-Pro-Ala-NH2/100 mL), and 25 .mu.L thrombin inhibitor soln. (127.6 mg CRC 200/100 mL) was preincubated at 37.degree. for 1 min, 50 .mu.L .alpha.-thrombin soln. (4.2 .mu.g = 10 IU/mL) was added, and light transmission was

measured in an aggregometer as a function of time. The IC50 for the thrombin inhibitor measured by this method was 10 nM.

IC ICM C12Q001-56
ICS G01N033-86

CC 9-2 (Biochemical Methods)

ST platelet aggregation **detn thrombin inhibitor** ; fibrin coagulation inhibitor platelet aggregation detn

IT Fibrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(coagulation, inhibitors of; method for detn. of thrombocyte aggregation)

IT Peptides, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fibrin aggregation inhibitors; method for detn. of thrombocyte aggregation)

IT Blood platelet
Blood platelet aggregation inhibitors
(method for detn. of thrombocyte aggregation)

IT 47295-77-2 67869-61-8 67869-62-9 135679-88-8
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fibrin aggregation inhibitor; method for detn. of thrombocyte aggregation)

IT 9002-04-4, **Thrombin**
RL: ANT (Analyte); ANST (Analytical study)
(**inhibitors**; method for **detn**. of thrombocyte aggregation)

IT 146663-95-8, CRC 200
RL: ANT (Analyte); ANST (Analytical study)
(**thrombin inhibitor**; method for **detn**. of thrombocyte aggregation)

L13 ANSWER 12 OF 54 CA COPYRIGHT 2003 ACS

AN 122:127572 CA

TI Hirudin analogs and their therapeutic, prophylactic and diagnostic uses

IN De Rosa, Alfredo; Rossi, Armando

PA Development Biotechnological Processes S.N.C. di Pelliccia Maria Teresa, Italy

SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9424156	A1	19941027	WO 1994-EP1144	19940413
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2160537	AA	19941027	CA 1994-2160537	19940413
	AU 9465683	A1	19941108	AU 1994-65683	19940413
	JP 08512020	T2	19961217	JP 1994-522738	19940413
	EP 804470	A1	19971105	EP 1994-913591	19940413
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	US 5723576	A	19980303	US 1995-532567	19951016
PRAI	IT 1993-MI748		19930416		
	WO 1994-EP1144		19940413		

AB Peptides having 25 to 27 amino acids capable of binding both to the catalytic site and to the non-catalytic site of hirudin are described. Pharmaceuticals contg. the peptides; invasive prostheses coated with the peptides; diagnostic kits for detg. concns. of factors IXa or Xa and of thrombin; and, the peptides labeled with a radioisotope for ex vivo

imaging of thrombi are claimed. Five 26-amino acid hirudin analogs (hirunorms) were prepd. and tested for efficacy in increasing activated partial thromboplastin time, prothrombin time, and thrombin time and in inhibiting platelet aggregation, as well as for their resistance to plasma proteases. The analogs generally were more active than hirudin.

IC ICM C07K007-10
ICS A61K037-64; G01N033-86; A61L027-00

CC 7-3 (Enzymes)
Section cross-reference(s): 63

ST hirudin analog hirunorm thrombin inhibitor

IT Thrombus and Blood clot
(fibrin or platelet; radiolabeled hirudin analogs with thrombin inhibitor activity for ex vivo imaging of thrombi)

IT Prosthetic materials and Prosthetics
(invasive; hirudin analogs with thrombin inhibitor activity for coating of prostheses)

IT 160588-92-1 160588-93-2 160588-94-3 160588-95-4 160588-96-5
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; hirudin analogs and their therapeutic, prophylactic and diagnostic uses)

IT 8001-27-2DP, Hirudin, analogs
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hirudin analogs and their therapeutic, prophylactic and diagnostic uses)

IT 9002-04-4, Thrombin 9002-05-5, Factor Xa 37316-87-3, Blood-coagulation factor IXa
RL: ANT (Analyte); ANST (Analytical study)
(hirudin analogs with **thrombin inhibitor** activity for **detn.** of blood coagulation factors)

L13 ANSWER 13 OF 54 CA COPYRIGHT 2003 ACS

AN 120:128519 CA

TI Test for quantitative thrombin time

IN Reid, Thomas; Alving, Barbara; Hendricks, Glenna

PA Department of the Army, U.S. Government, USA

SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9325578	A1	19931223	WO 1993-US5315	19930603
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5476771	A	19951219	US 1993-21033	19930222
	AU 9347681	A1	19940104	AU 1993-47681	19930603
	EP 643727	A1	19950322	EP 1993-918119	19930603
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08501682	T2	19960227	JP 1993-501586	19930603
PRAI	US 1992-893631		19920605		
	US 1993-21033		19930222		
	WO 1993-US5315		19930603		

AB A quant. method for detg. the plasma levels of thrombin-sp. inhibitors is based on the quant. thrombin time using plasma dilns., excess fibrinogen, and thrombin. The plasma dilns. and excess fibrinogen act in concert to eliminate the effects that coagulopathies have on std. coagulation tests. The method is relatively simple and provides superior results to std. conventional tests. The method is suitable for performance in clin. hematol. labs. on a routine basis using com. available instrumentation. Quant. thrombin times are compared to std. thrombin times and APTT data for several coagulopathies. Validity of the quant. thrombin time in detg.

plasma recombinant hirudin levels was assessed.
IC ICM C07K007-10
ICS C07K007-08; A61K009-22; A61K031-445; A61K037-00; A61K037-02; A61K037-43
CC 7-3 (Enzymes)
Section cross-reference(s): 9
ST quant thrombin time **thrombin inhibitor detn**; hirudin detn quant thrombin time; coagulopathy quant thrombin time; fibrinogen excess quant thrombin time
IT Phospholipids, biological studies
RL: BIOL (Biological study)
(antibody to, quant. thrombin time for removal of interference from)
IT Fibrinogens
RL: BIOL (Biological study)
(blood plasma diln. and excess, for quant. thrombin time)
IT Blood plasma
(diln. of, excess fibrinogen and, for quant. thrombin time)
IT Dilution
(of blood plasma sample, excess fibrinogen and, for quant. thrombin time)
IT Fibrinogen degradation products
RL: BIOL (Biological study)
(quant. thrombin time for removal of interference from increased)
IT Antibodies
RL: BIOL (Biological study)
(to phospholipid, quant. thrombin time for removal of interference from)
IT Blood coagulation
(disorder, quant. thrombin time for removal of interference from)
IT Fibrinogens
RL: BIOL (Biological study)
(metabolic disorders, dysfibrinogenemia, quant. thrombin time for removal of interference from)
IT Protamines
RL: BIOL (Biological study)
(sulfates, quant. thrombin time with blood plasma diln. and excess fibrinogen and, as neutralizing agent for heparin)
IT 8001-27-2, Hirudin
RL: BIOL (Biological study)
(detn. of recombinant, quant. thrombin time for)
IT 9001-30-3, Blood-coagulation factor XII
RL: BIOL (Biological study)
(quant. thrombin time for removal of interference from low)
IT 9005-49-6, Heparin, biological studies
RL: BIOL (Biological study)
(quant. thrombin time with blood plasma diln. and excess fibrinogen and neutralizing agent for)
IT 9002-04-4, Thrombin
RL: BIOL (Biological study)
(time, quant., plasma diln. and excess fibrinogen in)

L13 ANSWER 14 OF 54 CA COPYRIGHT 2003 ACS
AN 120:101262 CA
TI Test for quantitative thrombin time for quantitating thrombin inhibitors using plasma dilutions and excess fibrinogen
IN Reid, Thomas J., III; Alving, Barbara M.
PA USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9325220 A1 19931223 WO 1993-US5297 19930602
W: AU, CA, JP, KR
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
US 5476771 A 19951219 US 1993-21033 19930222
AU 9344052 A1 19940104 AU 1993-44052 19930602
PRAI US 1992-893631 19920605
US 1993-21033 19930222
WO 1993-US5297 19930602

AB A quant. method for detg. the plasma levels of thrombin-sp. inhibitors is based on the quant. thrombin time (QTT) using plasma dilns., excess fibrinogen, and thrombin. The plasma dilns. and excess fibrinogen act in concert to eliminate the effects that coagulopathies have on std. coagulation tests. The method is relatively simple and provides superior results to std. conventional tests. The method is suitable for performance in clin. hematol. labs. on a routine basis using com. available instrumentation. A std. curve for recombinant hirudin was prepd. using the QTT in which plasma samples supplemented with various amts. of hirudin were dild. 1:10 in buffer, 100.mu.L of dild. plasma was added to 100.mu.L human fibrinogen and incubated for 30 s, 100.mu.L of human .alpha.-thrombin was added to start the reaction, and the clotting time was measured.

IC ICM A61K037-02
ICS A61K031-445; C07K007-08; C07K007-10

CC 9-2 (Biochemical Methods)
Section cross-reference(s): 1, 7

ST **thrombin inhibitor detn** fibrinogen; blood plasma diln thrombin inhibitor assay

IT Fibrinogens
RL: ANST (Analytical study)
(**thrombin inhibitors detn**. in blood plasma by plasma diln. and thrombin and excess)

IT Blood analysis
(**thrombin inhibitors detn**. in, blood plasma diln. and excess fibrinogen in)

IT Protamines
RL: ANST (Analytical study)
(sulfates, **thrombin inhibitors detn**. in blood plasma by plasma diln. and excess fibrinogen and thrombin in presence of heparin using, as neutralizing agent)

IT 8001-27-2, Hirudin
RL: ANST (Analytical study)
(detn. of recombinant, in blood plasma, plasma diln. and excess fibrinogen and thrombin in)

IT 9002-04-4, **Thrombin**
RL: ANST (Analytical study)
(**inhibitors** of, **detn**. of, in blood plasma, plasma diln. and excess fibrinogen and .alpha.-thrombin in)

IT 9005-49-6, Heparin, uses
RL: USES (Uses)
(**thrombin inhibitors detn**. in blood plasma by plasma diln. and excess fibrinogen and thrombin in presence of, neutralizing agent for)

L13 ANSWER 15 OF 54 CA COPYRIGHT 2003 ACS
AN 119:155501 CA
TI Determination of hirudin and synthetic thrombin inhibitors
IN Nowack, Goetz; Bucha, Elke; Hoffmann, Jutta
PA Max-Planck-Gesellschaft zur Foerderung der Wissenschaften eV, Germany
SO Ger. Offen., 8 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	DE 4203980	A1	19930812	DE 1992-4203980	19920211
	WO 9316390	A1	19930819	WO 1993-EP161	19930125
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 626070	A1	19941130	EP 1993-903232	19930125
	EP 626070	B1	19960403		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, SE				
	JP 07503373	T2	19950413	JP 1993-513708	19930125
	JP 3198111	B2	20010813		
	AT 136367	E	19960415	AT 1993-903232	19930125
	ES 2087715	T3	19960716	ES 1993-903232	19930125
	US 5547850	A	19960820	US 1994-284453	19941005
PRAI	DE 1992-4203980	A	19920211		
	WO 1993-EP161	W	19930125		

AB Hirudin and synthetic thrombin inhibitors are detd. in blood or blood components by addn. of a prothrombin intermediate (e.g. meizothrombin) and/or a substance which cleaves prothrombin to meizothrombin (e.g. snake venom) and measuring the clotting time. Thus, 0.40 mL blood contg. hirudin was mixed with 0.1M CaCl2 0.02, ecarin (200 U/mL) 0.02, and 0.05M Tris buffer (pH 7.4) 0.16 mL at 37.degree. in an automated coagulometer. The coagulation time increased with increasing hirudin concn.

IC ICM C12Q001-56
ICS G01N033-80

ICA C12Q001-37; C12N009-99

CC 9-2 (Biochemical Methods)
Section cross-reference(s): 7

ST hirudin detn blood prothrombin intermediate; **thrombin inhibitor detn** prothrombin intermediate; meizothrombin **thrombin inhibitor detn** blood

IT Blood analysis
(hirudin detn. in, by coagulometry, prothrombin-thrombin conversion intermediates in)

IT Venoms
(of snake, in hirudin detn. in blood)

IT Snake
(venom of, in hirudin detn. in blood)

IT 12001-79-5, Vitamin K
RL: ANST (Analytical study)
(antagonists, meizothrombin induced by, in hirudin detn. in blood)

IT 9001-26-7, Prothrombin
RL: PROC (Process)
(conversion of, to thrombin, intermediates in, in hirudin detn. in blood)

IT 8001-27-2, Hirudin
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in blood by coagulometry, prothrombin-thrombin conversion intermediates in)

IT 55466-26-7, Ecarin 69346-19-6, Meizothrombin 105881-83-2, Meizothrombin (des F1)
RL: ANST (Analytical study)
(in hirudin detn., in blood)

IT 9002-04-4, **Thrombin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors, detn.** of, in blood by coagulometry, prothrombin-thrombin conversion intermediates in)

L13 ANSWER 20 OF 54 CA COPYRIGHT 2003 ACS

AN 107:232195 CA

TI Method and reagents for spectrophotometric determination of proteinase inhibitors in solution or blood

IN Kolde, Hans Juergen

PA Behringwerke A.-G., Fed. Rep. Ger.

SO Ger. Offen., 13 pp.

CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3531778	A1	19870312	DE 1985-3531778	19850906
	EP 216179	A1	19870401	EP 1986-111844	19860827
	EP 216179	B1	19910821		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 66493	E	19910915	AT 1986-111844	19860827
	ES 2000974	A6	19880401	ES 1986-1611	19860904
	US 4918001	A	19900417	US 1986-903458	19860904
	DK 8604255	A	19870307	DK 1986-4255	19860905
	AU 8662367	A1	19870312	AU 1986-62367	19860905
	AU 611847	B2	19910627		
	JP 62061600	A2	19870318	JP 1986-208109	19860905
	CA 1292174	A1	19911119	CA 1986-517638	19860905
PRAI	DE 1985-3531778		19850906		
	EP 1986-111844		19860827		

AB Proteinase inhibitors in soln. are detd. spectrophotometrically in the presence of a substrate (e.g. chromogen- or fluorescent substance-peptide conjugate) and an appropriate proteinase. The amt. of inhibitor present is related to the rate of hydrolysis of the label from the peptide. A std. curve was obtained for antithrombin III with a normal blood plasma sample using D-Phe-Pro-Arg-5-amino-2-nitrobenzoic acid isopropylamide (I) as substrate and .alpha.-thrombin as proteinase in a buffered reaction soln. contg. heparin. The difference in absorbance (405 nm) at 90 s and 15 s after initiation of enzymic reaction at varying concns. of I was plotted against varying dilns. of the blood sample. The antithrombin III concns. in 20 pathol. plasma samples were detd. by the above method using the derived curve, and the values were in good agreement with those obtained by a std. technique.

IC ICM C12Q001-38
ICS C12Q001-56
CC 7-3 (Enzymes)
Section cross-reference(s): 14
ST proteinase inhibitor detn; antithrombin detn thrombin labeled peptide; blood proteinase inhibitor detn spectrophotometry
IT Blood analysis
(proteinase inhibitor detn. in, spectrophotometric, proteinase and labeled peptide for)
IT Spectrochemical analysis
(spectrophotometric, proteinase inhibitor detn. by, proteinase and labeled peptide in)
IT 60457-00-3 82564-18-9 91999-42-7 93739-46-9 96559-87-4 111542-03-1
RL: BIOL (Biological study)
(as substrate in proteinase inhibitor spectrophotometric detn.)
IT 9000-94-6 9041-92-3, .alpha.1-Trypsin inhibitor 37205-61-1, Proteinase inhibitor
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, spectrophotometric, proteinase and labeled peptide in)
IT 9005-49-6, Heparin, uses and miscellaneous
RL: USES (Uses)
(in proteinase inhibitor spectrophotometric detn.)
IT 9001-92-7, Proteinase 9002-04-4, **Thrombin**
RL: BIOL (Biological study)
(**inhibitor detn.** with labeled peptide and, spectrophotometric)
IT 9004-07-3, Chymotrypsin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, detn. of, spectrophotometric, chymotrypsin and labeled peptide in)

IT 80295-70-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, detn. of, spectrophotometric, esterase and labeled peptide in)
IT 9001-01-8, Kallikrein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, detn. of, spectrophotometric, kallikrein and labeled peptide in)
IT 9002-05-5, Factor Xa
RL: BIOL (Biological study)
(proteinase inhibitor detn. with labeled peptide and, spectrophotometric)
IT 9004-06-2, Elastase
RL: BIOL (Biological study)
(.alpha.1-trypsin inhibitor detn. with labeled peptide and, spectrophotometric)

L13 ANSWER 21 OF 54 CA COPYRIGHT 2003 ACS
AN 107:146680 CA
TI HPLC **determination** of the synthetic **thrombin inhibitor** N.alpha.-(2-naphthylsulfonylglycyl)-4-amidinophenylalanine piperidide in biological material
AU Paintz, M.; Richter, M.; Hauptmann, J.
CS Inst. Pharmal. Toxicol., Med. Acad. Erfurt, Erfurt, Ger. Dem. Rep.
SO Pharmazie (1987), 42(5), 346
CODEN: PHARAT; ISSN: 0031-7144
DT Journal
LA English
AB The title compd. I was detd. in bile and liver homogenates by HPLC on Separon SIX C18 with MeCN-H2O-HClO4 as the mobile phase and detection at 235 nm. Rat liver homogenate was extd. in several steps with CHCl3-iso-PrOH; rat and rabbit bile was used directly after diln. The recovery of I from the homogenate was 32.8%. No metabolites of I were detected in the chromatogram, and the HPLC data agreed satisfactorily with a bioassay for I. The described procedure is recommended for the detn. of I and other benzamidine derivs.
CC 1-1 (Pharmacology)
ST benzamidine deriv detn bile liver HPLC; naphthylamidinopiperidine detn biol material HPLC; liq chromatog benzamidine deriv
IT Bile
Body fluid
Liver
Organ
((naphthylsulfonylglycyl)amidinophenylalaninylpiperidine detn. in, by HPLC)
IT Chromatography, column and liquid
(high-performance, of benzamidine derivs., in biol. material)
IT 618-39-3D, Benzamidine, derivs. 86845-59-2
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in biol. material by HPLC)

L13 ANSWER 24 OF 54 CA COPYRIGHT 2003 ACS
AN 95:75917 CA
TI **Determination** of **thrombin inhibitors** by an amidolytic method. Comparison of three substrates
AU Rybak, M.; Simonianova, E.; Kasafirek, E.
CS Ustav Hematol. Krevni Transfuse, Prague, 12820, Czech.
SO Biochemia Clinica Bohemoslovaca (1980), 9(1), 67-73
CODEN: BCBHAJ; ISSN: 0139-9608
DT Journal
LA Czech
AB Antithrombin III was detd. in blood plasma with tosyl-Gly-Pro-Arg p-nitroanilide (I), tosyl-Phe-Val-Arg p-nitroanilide (II), and benzoyl-Phe-Val-Arg p-nitroanilide (III) as substrates. Com. thrombin

prepns. (Topostasin and IMUNA) were used after removal of other serine proteinases on a Sephadex column. The thrombin reaction was measured under zero-order conditions (excess substrate) for a period of .gtoreq.3-5 min during the linear time-dependent hydrolysis. A convenient enzyme/substrate ratio was defined and the procedure verified with partially purified antithrombin III and a series of diln. curves of human plasmas. I and III were effective substrates for plasma antithrombin detn., whereas II yielded different results and was unable to detect small fluctuations in antithrombin level.

CC 7-1 (Enzymes)

ST **thrombin inhibitor detn** amidolysis; antithrombin detn plasma amidolysis

IT Blood analysis
(antithrombin III amidolytic detn. in)

IT 9000-94-6
RL: BIOL (Biological study)
(III, detn. of, in blood plasma, amidolytic method for)

IT 54799-93-8 65316-83-8 73945-44-5
RL: BIOL (Biological study)
(in antithrombin III detn.)

L13 ANSWER 26 OF 54 CA COPYRIGHT 2003 ACS

AN 90:117085 CA

TI Determination of antithrombin activity by an amidolytic and a clotting procedure

AU Frigola, A.; Angeloni, S.; Cerqueti, Anna Rita

CS Lab. Clin. Pathol., B. Eustachio Hosp., San Severino Marche, Italy

SO Journal of Clinical Pathology (1979), 32(1), 21-5
CODEN: JCPAAK; ISSN: 0021-9746

DT Journal

LA English

AB Plasma antithrombin activity was measured using an amidolytic method (substrate, Chromozym TH) and a clotting method. The mean antithrombin values found in 76 hospital out-patients were 9.4 .mu.mol/min/mL with the amidolytic procedure and 100.1% of antithrombin activity with the clotting procedure. The 2 methods correlated fairly well ($r = 0.85$, $p < 0.01$) and showed satisfactory reproducibility. Coeffs. of variation of 5.9% and 8.8% were obtained, resp., with the amidolytic and the clotting procedures. In the presence of very high levels of fibrinogen degrdn. products, falsely elevated antithrombin activity levels were obsd. with the clotting procedure, but the amidolytic method was essentially unaffected. It was concluded that both methods are suitable for detg. antithrombin activity, but a well-standardized amidolytic procedure has some advantages.

CC 7-3 (Enzymes)

ST antithrombin III detn plasma; **thrombin inhibitor detn** plasma

IT Blood analysis
(antithrombin III detn. in)

IT 9000-94-6
RL: BIOL (Biological study)
(III, detn. of, in blood plasma)

L13 ANSWER 27 OF 54 CA COPYRIGHT 2003 ACS

AN 87:196025 CA

TI Enzymic **determination** of thrombin and **thrombin inhibitors**

AU Roth, M.; Haarsma, M.

CS Lab. Cent., Hop. Cantonal, Geneva, Switz.

SO New Methods Anal. Coagulation Using Chromogenic Substrates, Proc. Symp. Dtsch. Ges. Klin. Chem. (1977), Meeting Date 1976, 91-104. Editor(s): Witt, Irene. Publisher: de Gruyter, Berlin, Ger.
CODEN: 36PUAG

DT Conference

LA English
AB Blood plasma prothrombin was assayed with the use of the chromogenic substrates, N-carbobenzyloxy-Gly-Pro-Arg-p-nitroanilide (Chromozym TH) or benzyl-Phe-Val-Arg-p-nitroanilide (S-2160). Prothrombin was converted into thrombin by thromboplastin with Ca2+ or Simplastin automated, and substrate hydrolysis was continuously followed with a recording spectrophotometer. Thrombin was assayed in 125-625-fold dild. human blood plasma after the addn. of thromboplastin. Inhibition of thrombin activity by pretreatment with a mixt. of defibrinated plasma and heparin is a convenient index of plasma antithrombin.
CC 7-1 (Enzymes)
ST thrombin antithombin detn blood; prothrombin detn blood
IT 9000-94-6 9001-26-7 9002-04-4
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, spectrophotometric)
IT 9005-49-6, uses and miscellaneous
RL: USES (Uses)
(in antithrombin detn.)
IT 38789-84-3 61906-49-8
RL: BIOL (Biological study)
(in thrombin and antithrombin detn.)

L13 ANSWER 28 OF 54 CA COPYRIGHT 2003 ACS
AN 85:42690 CA
TI Method for the simultaneous determination of precursors of kallikrein, plasmin, thrombin and their inhibitors in human blood plasma
AU Gomazkov, O. A.; Komissarova, N. V.
CS Inst. Gen. Pathol. Pathol. Physiol., Moscow, USSR
SO Byulleten Eksperimental'noi Biologii i Meditsiny (1976), 81(5), 632-4
CODEN: BEBMAE; ISSN: 0365-9615
DT Journal
LA Russian
AB Prekallikrein, plasminogen, and prothrombin of human blood plasma were sep. activated by kaolin, streptokinase, and thromboplastin. By measuring the (N-D-Tozyl-L-arginine Me ester, esterase activity of each enzyme and its changes in the course of plasma incubation with the activator, it was possible to est. the values of precursors of kallikrein, plasmin, thrombin, and their inhibitors. Evidence is given that under the conditions described, the activation is specific for each enzyme and does not affect the level of the other 2 precursors. The method may be used to det. the value of 7 parameters in 0.4-0.7 ml blood plasma.
CC 7-1 (Enzymes)
ST plasma kallikrein plasmin thrombin detn; kallikrein precursor inhibitor detn; plasmin precursor inhibitor detn; thrombin precursor inhibitor detn
IT Blood analysis
(kallikrein and plasmin and **thrombin inhibitors** and precursors **detn.** in)
IT 9001-26-7 9001-91-6
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in blood plasma)
IT 9001-01-8 9001-90-5 9002-04-4
RL: BIOL (Biological study)
(inhibitor and precursor of, detn. of, in blood plasma)

L13 ANSWER 29 OF 54 CA COPYRIGHT 2003 ACS
AN 82:27602 CA
TI Protease inhibitors
AU Fritz, Hans; Trautschold, Ivar; Werle, Eugen
CS Inst. Klin. Chem., Univ. Muenchen, Munich, Fed. Rep. Ger.
SO Methoden Enzym. Anal., 3. Neubearbeitete Erweiterte Aufl. (1974), Volume 1, 1105-22. Editor(s): Bergmeyer, Hans Ulrich. Publisher: Verlag Chem., Weinheim/Bergstr., Ger.
CODEN: 29GMAP
DT Conference; General Review

LA German
AB A review with 43 refs., of spectrophotometric methods for the detn. of protein proteinase inhibitors.
CC 7-0 (Enzymes)
ST review proteinase inhibitor detn; trypsin inhibitor detn review; plasmin inhibitor detn review; chymotrypsin inhibitor detn review; kallikrein inhibitor detn review; **thrombin inhibitor detn** review
IT 9035-81-8 37205-61-1
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, spectrophotometric)
IT 9001-01-8 9001-90-5 9002-04-4 9004-07-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, spectrophotometric detn. of)

L13 ANSWER 45 OF 54 CA COPYRIGHT 2003 ACS
AN 47:66463 CA
OREF 47:11298i,11299a
TI A method for the separate **determination** of **thrombin inhibitor** and antithrombin
AU Witte, Siegfried; Dirnberger, Paul
CS Univ. Wurzberg, Germany
SO Klinische Wochenschrift (1953), 31, 598-600
CODEN: KLWOAZ; ISSN: 0023-2173
DT Journal
LA Unavailable
AB The method is based on measuring the thrombin-inactivating capacity of native and defibrinated plasma. The difference between the 2 values is a measure of thrombin inhibitor. The amt. of thrombin remaining in incubated defibrinated plasma is a measure of antithrombin.
CC 11B (Biological Chemistry: Methods and Apparatus)
IT Blood
(analysis, **detn.** of **thrombin inhibitor**)
IT 9002-04-4, **Thrombin**
(**inhibitors** of, **detn.** of antithrombin and)